VORTRÄGE UND AUFSÄTZE ÜBER
ENTWICKELUNGSMECHANIK DER ORGANISMEN
HERAUSGEGEBEN VON **WILHELM ROUX**

7

HEFT XII

AUTOKATALYTICAL SUBSTANCES

THE DETERMINANTS

FOR THE INHERITABLE CHARACTERS

A BIOMECHANICAL THEORY
OF INHERITANCE AND EVOLUTION

BY

DR. AREND L. HAGEDOORN
VERRIÈRES-LE-BUISSON (FRANKREICH)

LEIPZIG
VERLAG VON WILHELM ENGELMANN
1911

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ENTWICKELUNGSMECHANIK DER ORGANISMEN

UNTER MITWIRKUNG VON

PROF. D. BARFURTH, ROSTOCK, PROF. E. BATAILLON, DIJON, PROF. BENEKE, HALLE A/S., PROF. TH. BOVERI, WÜRZBURG, PROF. H. BRAUS, HEIDELBERG, PROF. C. M. CHILD, CHICAGO, PROF. YV. DELAGE, PARIS, PRIV.-DOC. DR. DR. DRIESCH, HEIDELBERG, PROF. A. FISCHEL, PRAG, Prof. R. FUCHS, ERLANGEN, PROF. W. GEBHARDT, HALLE, PROF. E. GODLEWSKI JUN., KRAKAU, PROF. GR. HARRISON, NEW HAVEN, PROF. C. HERBST, HEIDELBERG, Prof. AM. HERLITZKA, TURIN, PROF. E. KÜSTER, KIEL, PROF. J. LOEB, NEW YORK, PROF. O. MAAS, MÜNCHEN, PROF. T. H. MORGAN, NEW YORK, PRIV.-DOC. H. PRZIBRAM, WIEN, PROF. RHUMBLER, MÜNDEN, PROF. E. SCHWALBE, ROSTOCK, PROF. SPEMANN, ROSTOCK, PROF. STRASSER, BERN, PROF. TORNIER, BERLIN, PROF. EDM. WILSON, NEW YORK, UND ANDEREN

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1. Introduction.

There is hardly any other question, for the answering of which so many totally different theories have been proposed, as the old one as to the way in which we have to picture the development of the germ into the individual with all its diverse qualities.

To an outstander it must look incomprehensible how from the same body of facts can have resulted two so absolutely opposed views as on one hand the biomechanical one, that the qualities of the organisms result in the develmopent of a comparatively simple germ under the influence of different forces inside and outside of it, and on the other hand the view of Weismann and de Vries, that all the characters of the organisms are predetermined in the germ by the existence of representative particles.

The only reason which admits of this enormous diversity of theories of evolution and heredity is the simple one, that we have been lacking facts.

Only because of the absence of all positive knowledge as to whether there exist such things as separately inheritable characters, in some way independent from each other, has it been possible for theorists to leave their imagination free play. Only therefore have we had such theories as Weismann's that in the germplasm there exist numerous small, living, protoplasmic particles of different kinds, each kind representing and calling forth in development one special kind of organ or tissue, and O. Hertwig's that the characters are exclusively the result of the reaction of a non-specialized germ on the conditions it encounters in its progression through development. Some years ago these and similar theories seemed equally incapable of direct proof and it has long been nearly a question of taste or of education, whether one felt more inclined toward the one or toward the other.

Much of the great difference between the two opposed views as to the mechanics of ontogenesis, heredity and evolution is doubtless due to the circumstance, that the two schools do not concern themselves with the study of quite the same group of phenomena. The biomechanists are in the first place interested in ontogenesis, and because they have found, in the comparatively recent enormous progress of their branch of science, the analytical study of development, how much the development of all organisms depends upon "external" conditions, some of them tend to underrate the importance of the study of the inheritable factors of development.

Weismann and the other Darwinists, on the other hand, parting from the consideration that the effects of the non-inherited factors of development are not transmitted, have had the tendency to ascribe all the qualities of the organisms which are the same for parent and offspring, to the activity of their purely hypothetical living particles, which are thought to be transmitted.

But the chief difficulty has been the lack of proof for one or the other of these views, and this very freedom from facts has made the purely speculative theories, such as Weismann's all the more imposing. What was needed above anything else was an answer to the question: Is there only one inherited factor for all the qualities of an organism or are there several, and if there are several inherited factors for the development of a germ into the organism with all its characters as we know it, in which way do these inherited factors contribute to the development, and what is their nature?

2. Mendelism.

An altogether new and already very fruitful field of inquiry into this particular question has been opened up by Mendel[1]). The method consists of studying each separately inheritable character in its turn by hybridization-experiments. Mendelists by this method have been able to make the three following important generalizations:

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[1]) Gregor Johann Mendel, Versuche über Pflanzen-Hybriden. Verh. Naturf. Verein Brünn, Band X, 1865, S. 1.

A. That to show any one hereditary character, an individual needs only inherit the corresponding hereditary factor from one of its parents.

B. That such an individual, which inherited some genetic factor for its development from only one parent furnishes one half the number of the gametes it produces with this thing, leaving the other half void of it.

C. That this distribution of the inheritable factor over one half the number of the gametes produced by a hybrid individual is as a rule not influenced by that of the other transmittable factors for the development.

It would lead us too far here to describe the numerous observations from which the above-named generalizations were deducted. I will give one illustrating example. There exists a variety of the domesticated rabbit which is white, and whose hair is very much longer than that of the ordinary rabbits. By a simple inspection of such a rabbit, or even by studying a whole family of such rabbits through many generations, one cannot decide whether these two qualities of this variety, white colour and long hair, are caused by a simple difference in the physico-chemical constitution of the germs of these rabbits, as compared with that of the germs of shorthaired and coloured ones, or else, that the whiteness and the longhairedness where each the result of either the presence or absence of something in the germ. When we now cross such a white longhaired animal with a coloured shorthaired one, we find that all the young resulting from this mating are coloured and have short hair. In this way we see, that it is sufficient if one parent be shorthaired and coloured to make a rabbit so. We know therefore, that, whether the difference between the two original forms be due to one thing or to more, the shorthaired coloured parent must have had this, the other must have lacked it.

To finally decide the question, we have to see how the hybrid individuals behave in the formation of gametes. As yet, we can only recognize the presence of the inherited factor necessary for the production of a quality by the production of this quality. It is as yet impossible to find these things in the germcells themselves. We must mate our hybrid individual to one whose gametes are certainly void of that which produces colour and short hair, in this case to a long-

haired white animal. If we do this, each young born will, as it were, be a representation of the gamete produced by the coloured shorthaired parent. In such a mating we find that one half of the number of young produced are coloured, the other half being white. Also, half the number is shorthaired, the other longhaired. And it are not again the white ones only which are longhaired, but the coloured and the white ones alike are longhaired and shorthaired in equal proportions.

Through this analysis we get to know positively that for each of the two conditions, shorthairedness and colour, there must be inherited a separate causating agent, capable of independent transmission.

3. Unitcharacters.

Through hybridization-experiments of this nature, we have been able to prove, that it are not the different varieties, the different biotypes (Johannsen) which we must consider as the units in inheritance, it are the characters which are capable of independent transmission. We have got to know an enormous number of such unit-characters, including the most diverse qualities of different organisms, such as cerebral hernia in poultry[1]), the ability of Mais endosperm to convert sugar into starch[2]), the female sex[3]), the presence of an accessory chromosome[4]), of pigment in the hair of mammals[5]). For a complete account of what has been done in this field I would advice the reading of Prof. W. Bateson's excellent book, Mendel's principles of heredity.

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1) C. B. Davenport, Inheritance in Poultry. Publ. Carn. Inst. No. 52, 1907.

2) C. Correns, Bastarde zwischen Maisrassen, mit besonderer Berücksichtigung der Xenien. Bibl. Bot. Original-Abh. a. d. G. der Bot. No. 53, 1901.

3) L. Doncaster, Sex Inheritance in the Moth Abraxas grossulariata. Report to the Evolution Comm. IV, 1908.

A. L. Hagedoorn, Mendelian inheritance of Sex. Archiv f. Entw.-Mech. 1909.

4) C. E. Mc Clung, The Accessory Chromosome. Biol. Bull. III, 1902.

5) L. Cuénot, La loi de Mendel et l'hérédité chez les souris. Arch. Zool. exp. et Gén. 1902, 03, 04, 05, 07.

How do we have to picture the action of these inherited factors? How do they cause the production of the characters? Is their presence enough to bring the character into existance? We must look for an answer to those cases, in which we have been able to study the way in which the characters originate. We know, that in the colour of flowers it is sometimes an oxydase which transforms the colour into another, or without which no colour is produced at all. This oxydase does not act in the way of Darwin's hypothetical pangens or Weismann's Iden. Its existance does not create the colour, it coöperates to its formation. In some white strains of flowers we know by breeding-experiments, that this oxydase can be present without producing colour, simply because that, which is modified by it, is missing. We can say, that generally a genetic factor for the development of an organism acts in changing something which already exists, into something else. One of the most interesting consequences of this seems to me to be, that the circumstances that such a genetic thing can only act in modifying an existing stage, gives an explanation of the fact, that in ontogenetic development the different qualities, that together make an organism like its parents, are acquired one after the other. It will, no doubt, be obvious, that an animal must first develop a tail to be able to show the white spots on that tail, that a tree must produce flowers to show the red colour of these flowers, but in other cases the necessity of the order in which one character is produced after the other, lies not so much on the surface.

The order, in wich ontogenetic development proceeds, is purely automatic. Only when a certain stage is reached, a given character can come into play. The order in which the characters follow each other in development is inherent in their nature.

Something in an embryo, which will cause the cells to migrate to the surface of the agglomeration of cells which results from the repeated divisions of the egg, can only become effective after a sufficiently large number of cells are formed. In the eight-cell or sixteen-cell stage all the cells are yet on the surface. In the next stage there may be cells which are no longer on the surface, and the migration begins, the blastula is formed.

Also, organs which are formed out of the alimentary tract of a very young embryo can not be formed before this alimentary tract exists. In a young sea-urchin gastrula, the thing, which by its action will widen out its digestive tract into a stomach, may very well be already present, the assumption even, that it would not already have been in the egg of yesterday, would be preposterous.

In this way, genetic factors acting upon already existing things will produce a result, which will in its turn be modified by still other genetic factors for the development. It would be possible to make a chemical model which would act in this way. We could make a combination of half a dozen different chemicals in which at first no action would take place. Under the influence of some external influence, e. g. agitation of the test-tube, B would act upon A, giving something different, X. This would be influenced by another chemical present, by C, so that Y resulted, and so on.

In this case it will not matter at all in which order the chemicals are poured into the test-tube. In any case they would only act upon each other in the order named.

This is obvious, and yet extremely important. For, the fact that in the embryological development of an organism, the different characters are always produced in the same regular order, has given rise to the remarkable hypothesis that this order is only a repetition of the order in which they were acquired by the strain to which the embryo belongs. It is said that the ontogenetic development is a picture of the phylogenetic development of the group. The theory goes under the name of Haeckel's Biogenetisches Grundgesetz. It must be remembered that the hypothesis dates from before the yet very recent development of the Biomechanics, inaugurated by Roux.

Recently some authors, Semon, Rignano and others, psycho-vitalists, have developed this theory and brought it to its logical consequences, the "memory" of all living matter, including germcells, which would enable an embryo to remember how its ancestors developed.

The theory was in its time, however curious it may look in its modern, psycho-vital garb, the only satisfactory way of dealing with the facts, that by each individual of a strain the same developmental stages are

passed. At present we can offer an alternative explanation, in the biomechanical view of development.

The theory of the analogy between ontogenetic and phylogenetic development is primarily based on the fact, that every single individual of a certain biotype will pass through all the same stages through which all the other individuals pass. It has been used to explain why certain forms go through stages of development which are final in other forms. These stages, it was held, were relics, vestiges of former existances, each of these stages having at some former period been the final stage of development.

4. Latent characters.

We know that the different unitcharacters, which go to make up the characteristics of the forms, are inherited separately, independently one from the other. But the resulting difference, the expression of the characters is quite another thing. The genetic factors for the production of a tail and the striping of the tail may be inherited independently, but it stands to reason, that whenever the genetic factor from whose coöperation the production of a tail depends, be absent and the resulting individual is tailless, the genètic, transmittable factor for the striping may well be present, but if so, stands small chance of getting expressed. As each genetic factor for the development acts only in modifying a stage of development, it necessarily follows, that the lack of any one of these factors may result in a number of other differences, depending from other factors, remaining inexpressed.

E. g. an animal's tail may be long, and hairy, and curled and striped with white, but if it be not produced, the curliness, and the striping and all its other qualities must necessarily be invisible. This does not mean that the genetic factors for the production of these qualities must be absent from the germ. The characters are not developed, not expressed, but their causating agents may well be there. In this way, and in no other, can characters become latent. Mind, the genetic factor for the development of this character is not carried in a "latent" condition. In the germ it is just as present as any other one. Only,

because some other factor misses in the germ, it can not be expressed in the developing individual, as its expression is solely through the modification of the stage which is reached under the influence of the other, now missing genetic factor.

In the formation of gametes, the transmittable causating agent for the latent character gets into the gamete just as well and just as functionally active as any other one. Therefore again, in the resulting individual the character will only be latent, when the stage which is modified by the genetic factor is again not reached because of the lack of the factors necessary for its production. If however these are present in the young individual, e. g. inherited from the other parent, the hitherto latent character will be again expressed.

From all this it follows, that there may be an exceedingly great number of things transmitted, which never coöperate to the development of the individuals. It might be, that in Paramoecium a genetic thing was transmitted from generation to generation, which thing would have the property of making an animal's tail curled or its teeth blunt. As, however, tail or teeth are not present, these things must wait their time.

Every time when, in crossing two biotypes, we get a hybrid which has properties, lacking in both its parents, we can be sure that these properties are due to the coöperation to the hybrid's development of genetic factors which could not act in the type in which they were present, because of the lacking of other things, which in the hybrid were given by the other parent. We have several instances of this. Bateson found, that in crossing two colourless types of Lathyrus, the hybrid was coloured (Mendel's Principles). Probably we have this same phenomenon in the sterile crosses between widely different forms such as the horse-ass cross and that between the canary and other finches. The very sterility of these hybrids can be explained in this way (Bateson, l. c.). From the order in which the characters of the organisms are produced we may not conclude anything as to the way in whith they got acquired.

We may picture the way in which the different genetic factors interact in development, by comparing the proceeding to the building

of a tower. First, the foundations must be laid. Only after these are in place the walls and buttresses can be erected. Only after the walls have reached a given height, can the lighter bricks be used for the upper part. The wooden superstructure can not be posed before this upper part is built up and finally the gilded weathervane and the tiles on the steeple can only be used after this superstructure is finished.

But all this gives us no clue as to the order in which all these building-materials arrived. It may be that by collections among the pious church-goers these things were acquired in the order in which they were needed. But equally well, some rich parishoners may have given the funds necessary for buying all the materials at once, or again, the beautiful gilt cock may have been the first thing donated.

How this may be, the materials can only be used in the order named. Not only will characters, which can only be expressed at the end of a certain development, always only be shown at that stage, be the genetic factors for their development acquired before or after the others, but if to-morrow any biotype were to lose any of its genetic factors, this loss would be felt at the stage in development modified by this factor, not at the end of its development.

We must not imagine the action of one of the genetic factors for the development of an organism to be that of changing the effect of that of the preceding one only. The result of the coöperation of any factor can be a modification of a great number of qualities. Along this line we must look for the explanation of correlations. If e. g. in Oenothera Lamarckiana, var. rubrinervis, we find an excessive brittleness of the stem, and at the same time a zigzag habit of the plant, we will have the look for a diminished number of woodfibres in the stem as a probable cause for both these qualities.

And many a quality, which we see the common property of all the individuals of a group, will only be the effect of a similar state of external conditions, always acting in the same way in coöperation with the genetic factors for the development.

5. Exceptions to Mendel's rules.

In the first years after the work of Mendel had been rediscovered by Correns and Tschermak[1]), and several authors had corroborated his statements, there has for some time been rather universally believed, that only a limited class of hereditary characters would "comply to Mendel's laws" and some authors have even tried to make generalisations as to which kind of characters would Mendelize and which would not. De Vries[2]) has elaborated the view that the difference between "varieties" are due to patency and latency, and those between species to presence and absence of characters. The effect of this distinction should be, that hybrids between varieties should show phenomena of Mendelian segregation in gameteformation and that the hybrids between species would remain stable in later generations. It has, however, been shown by some authors, that this apparent stability of the hybrids between widely different forms need not be due to any distinction between species and varieties, but simply to the fact that in some crosses we are dealing with two forms which differ in so many imperfectly known qualities, that under the individuals of the second generation, those combinations of characters, which would reproduce one of the parentforms, are so scarce as not to be included in a limited number of individuals. It stands to reason that if we do not know beforehand to how many genetic factors the difference between two forms is due, we can not tell how great a number of hybrids of the second generation must be observed to make it probable to see one presenting the same combinations of hereditable factors as shown by one of the parents.

If two forms differ in the possession or non-possession of n genetic factors for the development, we must have 4^n individuals of the second

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[1]) C. Correns, G. Mendels Regel über das Verhalten der Nachkommenschaft der Rassenbastarde. Ber. Deutsch. Bot. Gesellsch. XVII, Heft 4, S. 158, 1900.

E. Tschermak, Über künstliche Kreuzung bei Pisum Sativum. Zeitschrift f. d. landw. Versuchsw. in Österreich 1900, III. Jahrgang, Heft 5.

[2]) H. de Vries, Species and Varieties, their origin by Mutation, Chicago 1905, and: La loi de Mendel et les caractères constants des hybrides. C. R. 1903.

generation to have a chance of meeting one which is like either parent. For five of these hereditable factors, this necessary number becomes greater than thousand, for ten, it is already greater than one million.

For some reason or other, some of the earlier investigators have taken the reproduction of the parental types in the second generation as a criterium for "Mendelian Inheritance", irrespective of the limited number of individuals observed, so that in the earlier litterature on the subject exceptions to Mendel's rules were very numerous[1]). Needless to say that these exceptions, for so far as they have been reinvestigated, have been found to comply to the common rule, that each inherited factor, which is present in one parent only, is distributed by the hybrid to only half the number of the gametes it produces, irrespective of the distribution of the others.

Tschermak has found, that the hybrids between Secale cereale and S. montanum, between Barley and Hordeum spontaneum, between wheat and Aegilops, follow Mendelian rules.

I am indebted to Mr. de Vilmorin of Verrières for the occasion to study a number of descendants of a hybrid between Digitalis purpurea and Digitalis grandiflora. I examined the underside of the flower in these two species, and found that in Purpurea it was hairless, in Grandiflora it was hairy. These hairs were multicellular, and terminated in a gland.

The first hybrid plant had not been examined. Its descendants were 56 in number. I calculated, that if the multicellular hairs with the glands should be the result of the coöperation of three, independently transmitted, genetic factors, half the number of gametes of the hybrid plant, and therefore one fourth the number of plants in the second generation, would be without the factor necessary for the production of hairs. These must be hairless, irrespective as to whether they had or lacked the two other things. Of the remaining three quarter, again one fourth should have unicellular hairs, and of the plants with unicellular und multicellular hairs, each category should consist of such

[1]) A. Hagedoorn, Mendelian Inheritance of Sex. Arch. f. Entw.-Mech. 1909.

with glands (75 %) and such without (25 %). For 56 plants this would give the ratio: 14 hairless, 2,625 with unicellular glandless hairs, 7,875 with unicellular hairs with glands, 7,875 with multicellular hairs without glands, 23,6175 with multicellular hairs, terminating in a gland.

I now counted the five categories of plants, obtaining:

	Calculated	Observed.
Hairless	14	15
Unicellular without glands	2,625	2
Unicellular with glands	7,875	9
Multicellular without glands . . .	7,875	8
Multicellular with glands	23,625	22
Total:	56.	56.

This is as close to expectation as might be expected. In any case, a genetic factor inherited from only one parent had been distributed over half the number of gametes.

It has very often been forgotten that it are the genetic factors for the development of the organisms, which are the real units in heredity. When we are working with varieties or other sorts of biotypes as the units, we are bound to find all sorts of remarkable exceptions to the rules of independence of genetic factors.

De Vries has stated, that hybrids between what he calls "species" are stable, which statement I think, must be meaning that the hybrids between two such forms do not show phenomena of Mendelian segregation. But we see that in his own experiments, every time he does not regard these forms as units in inheritance, but gives his attention to some single characteristic of these forms, this character behaves like any other unitcharacter. As such we have got to know a character Brevistylis, caused by the absence of one genetic factor, and Nanella, caused by the absence of another. In 1908, de Vries[1]) published the results of crosses between Oenothera's in which again he dealt with unitcharacters or at least with biotypes differing in only two or three of these characters. The distribution of these characters is absolutely in accordance with the ordinary rule.

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[1]) Hugo de Vries, Über die Zwillingsbastarde von Oenothera nanella. Ber. der Deutsch. Bot. Gesellsch., Band XXXVIa, Heft 9.

Le Dantec[1]), a French author of semi-scientific works, has lately tried to "explain" the facts of segregation, by the assumption that it should be only the "ornamental" characters which follow these rules, such characters as have no value for the organism in the "struggle for existence". These characters, he thinks, are simply the result of the presence of bacteria in the organism which present them.

The idea, that only unimportant characters would obey Mendelian rules has some real foundation. We can not recognize the extent to which any one of the hereditable factors for the development of an organism modifies the development, and in consequence the qualities of this organism, unless we can compare an individual with this factor to one which has developed without it.

And the only way to be sure, that the external difference between two individuals is due to the presence or absence of one genetic factor, is to hybridize them and to study the way in which the inheritable factors are distributed over the gametes, produced by the hybrid[2]).

Now it stands to reason, that the only kind of characters, which can be analyzed, are those which depend from the presence of an inheritable factor, whose absence does not impare the life or the fertility of the individual. Suppose there exists a thing which in poultry is transmitted from parent to offspring, and whose presence is absolutely indispensable for the formation of an allantois by the embryo.

Those embryos which developed from eggs lacking this inherited factor would only develop up to a certain stage and die from suffocation. In this case we could never prove that the development of the allantois depended upon the presence of one essential, indispensable thing, simply because we can not mate an individual with to one without the organ.

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[1]) Le Dantec, La crise du Transformisme. Paris 1909.

[2]) E. Baur, Vererbungs- und Bastardierungsversuche mit Antirrhinum. Zeitschrift für induktive Abstammungs- und Vererbungslehre 1910 Bd. III.

George Harrison Shull, Germinal Analysis Through Hybridization. Proceedings Amer. Phil. Society, Vol. XLIX, No. 196, 1910.

But even if this limitation is unavoidable, we have abundant material to show that the most indispensable inherited things, as well as the less important, are transmitted in the same way, independently from others. We know, that in the deaf-born waltzing mice something is lacking, which permits of the normal development of the stria vascularis, further than to a very young stage, some days after the birth of the animal[1]). This abnormal development of the stria vascularis leads to a further abnormal development of the internal ear. From breeding-experiments we know that this transmittable something is inherited as one single thing, and independently from the inheritance of the other genetic factors in the animal's development.

Therefore, we know that the complex and important faculty of normal mice, to hear, and to walk normally, is depending on the presence in the germ of one single genetic factor, and therefore has the value of a unitcharacter.

One would hardly call the faculty of hearing and of normal progression ornamental characters, or things without value in the struggle for life. The same can be said of the faculty of the skin to produce pigment. Albinistic animals in a state of nature stand a very small chance of surviving.

We have no reason to suppose that only the numerous characters which happen to have been studied follow the general rule, whereas there should be others which would not.

6. Genetic and Non-genetic factors of development.

The analysis of the qualities of organisms into unitcharacters has taught us two things, firstly that there must be numerous inheritable factors for the development of an organism transmitted through the germ, and secondly that these genetic factors, as I have called them, to distinguish them from the non-genetic factors for the development, can not be representative determinants for the characters in Weismann's sense, but must be of such a nature, that at a definite stage in development they influence this, so that the final result is something different from what it should have been without the

[1]) Van Lennep, Nederlandsch Tydschrift voor Geneeskunde Nov. 1910.

cooperation of this genetic factor with the numerous other factors of the development of the organism.

We know that there must be numerous genetic factors for the development of an organism, but this does not mean, as Weismann has implied, that all the factors for development must be genetic, inherited ones.

Cope[1]) has stated as his belief, that the characters which are now due to inherited causes, have been due to influence of the surroundings, to use and disuse of organs, in short, to non-genetic causes of development, at some former period. And that the present effects of non-genetic factors will gradually become innate characters. Bringing this hypothesis to its logical conclusion, we would be forced to conclude that if only a group of organisms lived long enough subjected to the same unchanging external conditions, all the qualities of these organisms would finally assume a transmittable basis, and the organisms would become absolutely independent of their surroundings.

If in reality the effects of circumstances which favored the development of some organ, would in the course of some generations become transmitted to the offspring, and part of the genetic factors, this would result in a cumulative modification of the part affected by the external circumstance. For example, if the tail of a mouse got longer if the animal were raised in a high temperature, and this modification were hereditary in any way, so that the young of these mice, born and raised in the original temperature would have tails a little longer than those of normal mice (but we have no reason for such an assumption), this would have the effect that in the high temperature the young were born with an innate tendency to have a somewhat longer tail. Their tail would again be lengthened by the high temperature, and finally we would get the result, that in every generation the tail would get a little longer if the animals came to live in a permanently higher temperature. Finally, the tail of these mice would become enormously long, but composed of the original number of vertebrae, as this number is not affected by temperature.

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[1]) E. D. Cope, The primary factors of organic evolution. Chicago 1896.

The idea of Lamarck and the Lamarckists of the present day, that gradually those qualities of an organism, or of a family of organisms, which are due to a direct action of external influences of all kinds, including functional excitation, have assumed a material, transmittable basis, which later on suffices to produce the qualities even in the absence of those influences, rests on the assumption that the differences between the two kinds of variability, Modification through a more or less intense action of external influences, and Variation through a difference in the composition of the inheritable, transmittable causes for the development is a difference only of quantity, not a fundamental one.

If we say that there are two kinds of characters, inherited ones and such as depend on the action of external influences in the widest sense, it must be understood that this only is a way of expressing that the qualities of an organism as we know it, are the result of two causes, the constitution of the germ and the environment influencing the developing germ, the genetic and the non-genetic factors of development. My genetic factors of development correspond to the "Determinationsfactoren" of Roux[1]), my nongenetic factors to his "Realisations- and Alterationsfactoren".

Each quality is always the result of these two sets of causes. For example, the hairlength of the rabbit is partly due to the presence or absence of the genetic factor whose presence inhibits an otherwise continuous growth, partly to such influences as temperature, age and health of the animal.

These last factors are always variable, they are different for different animals, and their influence is such, that the length of the hair in a population of rabbits, all having the same set of genetic factors, fluctuates around a modal length. If however, we could keep all nongenetic influences constant, the hair in all the rabbits would have the same length.

In our case of hairlength in rabbits, the presence or absence of the genetic factor, inhibiting continuous growth, has such an enormous in-

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[1]) Wilhelm Roux, Die Entwickelungsmechanik, ein neuer Zweig der biologischen Wissenschaft. Heft I dieser Vorträge und Aufsätze 1905.

fluence, that the comparatively small fluctuations in length produced by the non-inherited causes can not mask the action of this genetic factor.

The hair of a rabbit with interrupted hairgrowth can, in a healthy individual and in low temperature become quite long, but it will never reach the length of that of a rabbit with a continuous hairgrowth, even if this latter is under unfavorable conditions.

But in other cases some genetic factor may have an effect which is comparatively slight if compared with the effects of the modifications by external influences. Johannsen[1]) has found in his experiments with beans, that the form of the seeds, the length-breadth index notably, as depending from genetic causes, is so much influenced by not-inheritable influences, such as the position in the pod, that the differences between seeds of plants, with the same set of genetic factors, are often greater than those produced by a different set of genetic factors.

In such instances it is often impossible to account for, how much of the difference between two individuals is due to genetic, how much to nongenetic factors of development, and this same difficulty makes it often impossible to study the influence of the genetic factors.

The only kind of variation which leads to inheritable differences is such as produces a difference in the set of transmittable causes for the development of an organism.

We can distinguish two different kinds of Variability:

A. Modification, the effect of the more or less intense action of causes not transmitted through the germ on the development. This effect of these modifications is limited to the individual which is altered by them.

B. Inheritable Variation, leading to transmittable differences in the set of genetic factors for the development.

Of the causes for inheritable Variation, we have already discussed

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[1]) W. Johannsen, Über Erblichkeit in Populationen und in reinen Linien, 1903.

one kind, the recombination of these genetic factors in the offspring of individuals whose parents differed in the possession or non-possession of some of these factors. We saw an instance of this in the production of coloured shorthaired, white shorthaired, coloured longhaired and white longhaired rabbits in the descendance of the hybrids between an albino longhaired and a coloured shorthaired rabbit.

This kind of genetic variability is very common, and has undoubtedly played an enormous part in the production of new forms in nature. There exists however a second kind of genetic variability, which has lately been the point of much discussion, the sudden production of organisms, differing from their parents in the constitution of their germ, apparently without cause. This kind of variability has severally been called "Mutation", "Discontinuous variation", "the production of sports". In our scheme we can provisionary classify it as genetic Variation from unknown causes.

To resume, this gives us:

A. Modification.

B. Variation through Mendelian segregation.

C. Variation through unknown causes.

Of the last-named kind of Variation, numerous instances are on record. In the accepting of these instances however, some caution is required. Undoubtedly, several cases of the production of new forms through a more or less complicated recombination of genetic factors in the offspring of hybrids, have been recorded as the effect of this kind or variation. Especially has this been the case before or shortly after the rediscovery of Mendel's work, when the possibilities of recombination of genetic factors were not yet, or still imperfectly, known. One such case has been the production of de Vries's new forms of Oenothera[1]) which I think is now generally accepted to be a rather complex case of Mendelian segregation.

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[1]) M. Leclerc du Sablon, De la nature hybride de l'Oenothère de Lamarck. Revue générale de Botanique XXIII, 1910.

W. Bateson, Mendel's principles of heredity. 1909.

A. Hagedoorn, Mendelian Inheritance of Sex. Roux' Archiv 1909.

We know, that the mere fact that a new biotype originated quite suddenly, may not be accepted as proof for its mutational origin[1]. A recombination of genetic factors can only be excluded as a possible explanation, when we are either working with organisms with asexual reproduction, or else if we can be very sure that the individual which produces the gamete from which one of the genetic factors is suddenly lacking, has inherited this genetic factor from both parents. This precaution has very often been neglected. The fact that so many more "sports" have been noted in plants than in animals, chiefly results, I think, from the circumstance that unnoticed hybridizations are nearly excluded in animals under domestication, whereas in plants they must be relatively common, even in habitual self-fertilizers. Of course, the finding of a sudden hereditable variation in a wild state may never be accepted as a true case of "sport", as the parents in such an instance are not available for the required test.

A sudden inheritable change in the set of genetic factors is theoretically possible in two different ways, either one or more genetic factors, common to the strain, may get lost, of else one or more new ones may be acquired. De Vries assumes the possibility of both these processes in his theory as to the origin of new forms of specific rank. But if we limit ourselves to the scientifically proved facts of the origin of individuals, differing from their parents in the genetic factors, we find that in every such an instance, this difference is due to the loss of only one of these factors at a time, never to anything else.

It would lead me too far here to discuss all the numerous cases of "sport" in detail, any one knowing the literature on the subject will have to concede that at least all those instances of a sudden inheritable difference between parent and offspring, in which any other explanation, even Mendelian segregation is rigourously excluded, conform to

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[1]) Über Modifikationen und experimentell ausgelöste Mutationen von Bacillus prodigiosus und anderen Chizophyten. Franz Wolff, Zeitschrift f. induktive Abstammungs- und Vererbungslehre, Band II, Heft 2, 1909.
A. Burk, Mutation bei einem der Koligruppe verwandten Bacterium. Archiv f. Hygiene 1908.

this general rule[1]). This rule, that the transmitted factors for the unitcharacters are sometimes lost, and if so, one at a time, is another proof for the mutual independence of these factors, whatever be their nature.

The genetic factors for the development of the organisms with all their qualities, must act, as we have seen, by making, when present, the development something different from what it should have been without their coöperation.

7. The material basis of the genetic factors.

How have we to picture to ourselves the mechanics of heredity and evolution? What is the nature of these genetic factors for the development of the organisms whose existance we are forced to admit by the facts of Mendelian Inheritance? Must we, now that we positively know that there exist separately transmittable causes for the directions of development, which lead to the production of specific qualities of these organisms, admit with Weismann and the other vitalists, that these transmittable things are vital particles, little globules of protoplasm, capable, among other things, of a multiplication by division? We will have to discuss the grounds on which Darwin and Weismann founded their theories, to see whether they do not admit of an other explanation, somewhat more in accordance with modern facts.

The central hypothesis of Darwin, that the determinants for the hereditary characters must be vital things, living granules, which can feed and multiply, has been retained in all the other theories of similar nature, that of de Vries and Weismann notably. It is not the superstructure built on this hypothesis which concerns us most here, it is the consideration whether it will be necessary to retain this idea.

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[1]) E. Baur, Vererbungs- und Bastardierungsversuche mit Antirrhinum l. c.

H. Nilsson-Ehle, Kreuzungsuntersuchungen an Hafer und Weizen. 1909.

F. Wolff, Über Modifikationen und experimentell ausgelöste Mutationen von Bacillus prodigiosus, l. c.

A. L. Hagedoorn, Origin of two varieties by one mutation in Mice. University of California public. 1908.

The facts force us to the conclusion, that in the germ there must be present things, which have been derived from the parent and are responsible, when present in the offspring, of making the individual develop differently from such as lack this thing.

We know further, that an individual, which has derived some of this inheritable something from at least one of its parents, therefore originally not more of it as can be present in this germcell, can produce so much of it, that it can furnish at least 50% of its germcells with enough of it to call forth the corresponding difference in development of the resulting organisms.

We also know that in many cases (it is merely a technical difficulty which prevents us from verifying this for all cases) these inheritable things must be present in all the cells of the individual. (One epidermis-cell of Begonia can give rise to a complete plant.) We are therefore forced to admit that the inheritable thing, with which we are dealing, is capable of reproducing its kind.

It is this consideration, which has led Darwin and his followers to conclude that therefore this thing must be living. It has seemed unavoidable to assume this vital nature of the determinants for the hereditable characters.

It is commonly taken for granted, that, as living things are protoplasmic, all things which show at least one of the properties of living things and which are at the same time parts of an organism, must therefore be themselves composed of protoplasm. To quote a good example of this way of reasoning from the book "Making of Species" by Dewar and Finn:

"The units which compose these molecules[1]) being made up of protoplasm are endowed with all the properties of life, including the inherent unstability which characterizes all living matter."

If we part from the principle that all the processes that take place in living beings must be vital phenomena, we must get this kind of reasoning, that all things, which are in the inside of a living being and

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[1]) A special kind of determinant or pangen, "biological molecules", for which the authors are responsible.

which have one characteristic in common with living things must therefore be vital things and "made up of protoplasm".

We might imagine someone who is used to this kind of reasoning, attentively dissecting a piece of plumpudding. He would in the inside of this piece find things which had several properties in common with boiled raisins, and he would say: "These things taste sweet, like plumpudding, moreover I have found them in plumpudding, and being an integral part of the plumpudding, therefore they must consist of plumpudding, and they cannot be raisins".

The reasoning that the determinants for the hereditary characters must be protoplasmic, because they are transmitted in a cell, and because we know that they must have the power of reproducing their kind, a quality of living beings, is not any less absurd than the one of the philosophical Christmasguest.

If we want to comprehend any complicated phenomenon like life, we must, as Roux has done, analyze "life" into its components, that is, we must try to become clear as to of which combination of properties consists the quality we call living. Afterwards, we must try to find out to which qualities of protoplasm or of its constituents are due these different properties which together make it living.

Roux has defined life as a complex of several, well characterized processes that all, directly or indirectly, serve to auto-conservation, that strengthen this auto-conservation by auto-regulation, and that are bound together by this auto-regulation to a higher unity.

We must again look to the facts to try and find whether there is not a possibility, that not the living being and "therefore" all the causating agents for its characters are living things, but that the organisms are living because of the fact that they have all these characters. The facts are simply these, that there must be things which are transmitted from a parent possessing a given quality, to the child, which things in the child are responsible for the appearance of the same qualities. These things, further, whatever they be, must be of such a nature, that when some one of them is present in the germ, the individual growing from it is able to distribute some of it to at least half the number of the germcells it produces.

The hypothesis that these hereditary things are vital units, composed of protoplasm and capable of assimilation and growth, certainly fits the facts. But we ask more of a theory of heredity and evolution. A working-hypothesis, to be of any use as an instrument of research, must explain the facts in terms of what is already known. It is inadmissable to try to explain the facts of evolution and inheritance by the behaviour of living particles which have been invented simply to admit of this explanation.

The making of a hypothesis must be a process, fundamentally different from that by which savages are wont to find explanations for meteorological phenomena (of the evil spirit kind).

If a hypothesis is not deduced from facts, and is not the simplest way of referring the greatest number of facts to what is already known, without any straining, it ceases to be a hypothesis and becomes a conjecture.

We know that the qualities of an organism result in the development of this organism under the influence of two sharply to be distinguished sets of causes, A the genetic factors for this development and B the nongenetic factors for the development, the different forces and circumstances which coöperate to the development, which modify it and make it possible.

We can distinguish these two sets of factors for the development only by analysis. Only if either one varies, the other remaining constant, can we get to know them separately. Variation of the nongenetic factors we see around us every day, the action of all the different external influences upon the development of one organism can hardly be exactly the same for a second one. Because these external influences of diverse kind are so very numerous and can each (temperature, atmospheric pressure, action of the food) vary in intensity, a population of individuals, having all the same set of genetic factors is bound to vary in the expression of all sorts of qualities, each quality fluctuating around a modal expression.

However important this kind of variability undoubtedly is for the individual which is modified by it, and however much its survival or death may depend upon it, we have abundant proof that the effects

of modifications can never be transmitted to the offspring. Originally it has been thought that this surprising circumstance was due to some sort of a difficulty for the effects of modifications to be transmitted to the cells from which ultimately the next generation is derived, and Weismann has even invented a cause for this difficulty, the hypothetical independence of "soma" and "germplasm". It must be remembered, that this hypothesis is inferred solely from the facts for the explanation of which it has been invented, as we have already discussed, an inadmissable proceeding, leading to nothing but word-play. It has been proved by experiments on unicellular organisms, that the effects of modifications in these organisms (Paramaecium, Jennings), where the daughter generation is a direct continuation of the parent one, are nevertheless as little transmitted as in multicellular organisms.

It follows from this, that selection on the effects of these modifications can never have any result. And this is actually the case. It has been found by Johannsen[1]), that a selection in a family in which all the members have the same set of genetic factors of development has absolutely no effect.

In America, at one of the breeding-stations, it has been tried to improve the egg-laying capacity of the common fowl by selection within a variety. This egg-yield depends to an enormous extent from such influences as age and health, housing, food and similar things. It was found that the daughters of selected hens, which had laid more than a certain very high number of eggs, were not any more liable to lay abundantly than those of the hens which did not come up to this standard.

The non-inheritance of modifications can therefore not be explained by an assumed independence of "soma" and "germplasm". There must be some fundamental difference between modifications and inheritable variations, which makes that these last alone are hereditary. Weismann's hypothesis of the gradual adaptation of organisms through natural selection on "fluctuating variability" can not be held, as this implies an inheritance of modifications, of the effects of the nongenetic factors of the development.

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[1]) W. Johannsen, Über Erblichkeit in Populationen und in reinen Linien. 1903.

Only the other kind of variability leads to hereditary differences. There is a difference between organisms which is not due to any greater or lesser influence of external conditions. Two individuals may differ in one or more unitcharacters, due to things which are transmitted through the germ. These transmittable factors are independent one from the other.

Their influence is not such as to "determine" any part or quality, they must be something sensibly different from the "determinants" of Weismann or the pangens of de Vries. We have analyzed a few cases in which it was visible that the influence of such a genetic factor is felt on some stage in the development. If the genetic factor is present at that stage, development proceeds in a certain direction, if the genetic factor be absent at that stage, development will lead to an ultimate product, different from what it should have been with the coöperation of this factor.

We have seen that genetic, inheritable variability is of two kinds. One cause of inheritable difference between parent and offspring is the fact that an individual, if it has inherited any one of these genetic factors from only one parent, in only one gamete, only furnishes one half the number of its gametes with it. Some of the offspring of such an individual have therefore one or more factors less than their parent. Or, they inherit still other genetic factors from the other parent, so that they become in this way different from the first one.

The other inheritable differences between parent and offspring is of a different nature. It happens that an individual which can be proved to have inherited some genetic factor from both parents (a homozygote in Mendelian language) nevertheless produces one or more gametes which are void of this factor. We have seen that we have no scientific proof for the occurrence of the opposite phenomenon, the appearance of a genetic factor in a germcell produced by an individual not having this factor.

These inheritable differences, the unitcharacters, are not necessarily large. They need not even be important for the individual. These unitcharacters can very easily be confounded with the effects of modifications, which are often considerably more important in determining the qualities of an individual. In such cases only scientific analysis by breeding tests can give us the answer.

8. Autokatalytical substances the inheritable factors.

What then is the nature of these genetic factors? We know that they can be transmitted separately, that they must be capable of reproducing their kind. They seem to be of such a nature that a new one can only be acquired by any form by a cross with another form having it, and never spontaneously.

We know that an individual which got one portion only, which inherited one of the factors from only one parent, generally shows the same influence as one inheriting the same thing from both parents, so that it seems that the initial quantity does not stand in a direct relation to the effect produced.

If these genetic things are not vital, living granules, or bacteria as Le Dantec frankly says, what can they be?

Roux[1]) assumes the existence in the fertilized ovum of 10—100 physico-chemical structural relations, that propagate themselves through their activation.

The genetic factors must be substances which in their cooperation admit of these conditions. It are these structural relations which give "body" to living things, and which if destructed cause its death. Thus things which have "body", like yeast-cells or bacillae of Tetanus can as such be destructed by passing them through a porcelain filter, although their components may pass the filter and propagate themselves like the cells, but very similar things, like the yeast of beer or "filterable viruses" like those which cause Rabies or Poliomyelitis pass unchanged through a filter.

I think that in those cases where unvisible things propagate themselves in the same way as visible organisms, it matters little whether bacteria are present or not. It is likely that what passes the filter is simply a chemical substance whith autokatalytical properties, or a combination of several of such substances. When we are dealing with bacteria or yeastcells these substances are bound

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[1]) Wilhelm Roux, Berliner klinische Wochenschrift 1909, No. 45. Referat über "Descendenz und Pathologie" von D. v. Hansemann.

together by structural relations (e. g. surface-tension and other forces), whereas in the pressed juice of yeastcells or in "filterable viruses" these substances, if there be more than one are not thus united.

I do not think that the possibility is excluded of creating "living" organisms by a combination of non-living things like the "filterable viruses" and other autokatalytical substances, in thus choosing them to create a system of structural relations, and thus a "body" for the combination.

Robertson[1]) has shown by a mathematical study of the rate of growth of organisms, that the acceleration of this growth is the same as that of the production of a substance which is a ferment for its own formation.

Parting from these considerations, Loeb[2]) has developed the hypothesis (pag. 232), that the nuclei of the different organisms differ in their chemical constitution, and that these chemical differences are the causes for the diversity in form of the different organisms. Every nucleus should be the ferment for its own synthesis, thus reproducing substance of its own kind. He supposes that this is the reason for the production by the hybrids of two kinds of germ-cells, such with a constitution like that of the hybrid's father, and such with a constitution like that of its mother. This idea is based on the assumption that in the formaton of germcells by a hybrid individual, the two halves of the nucleus, the paternal and the maternal half, separate again. We now know, from the numerous breeding-experiments which have been performed in the last ten years, that this conception of what happens in segregation can not be maintained, as it are not the parental types as such, which are reproduced by the hybrid, but it are the individual transmittable factors for all the characters in which the parents differ, which are distributed. The hypothesis that each biotype would be the result of a corresponding autokatalytical

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[1]) T. B. Robertson, On the normal rate of Growth of an Individual and its Biochemical significance. Archiv f. Entwicklungsmechanik XXV, 1908.

[2]) Jacques Loeb, Die chemische Entwicklungserregung des tierischen Eies. Berlin 1909.

substance, can not be held, but this does not mean that therefore the several transmitted factors for the development of a biotype should not be so many substances with autokatalytical properties.

My hypothesis, that the hereditary factors for the development of an organism are numerous independently transmitted substances, each having autokatalytical properties is therefore simply a modification of those of Loeb and Roux, necessitated by the facts of Mendelian inheritance.

It stands to reason, that the rate of development of an individual must be the same, whether the thing from whose formation this development depends be one simple autokatalytical substance or a mixture of several, all having autokatalytical properties.

9. Facts of heredity and evolution explained in the light of this hypothesis.

I will give a small list of the several facts of evolution and heredity which will have to be explained by any modern theory.

A. That there are two wholly different sets of factors for the development of the organisms, some of them genetic, transmitted from parent to offspring, the others, nongenetic.

B. That the genetic factors for the development of the organisms are transmitted independently one from the other.

C. That usually an individual, having acquired one genetic factor from only one parent, shows the effect of the coöperation of this factor to its development equally well as one which has acquired it from both parents.

D. That sometimes one of the genetic factors is omitted from a germcell produced by an individual which normally furnishes all gametes with it (a homozygote), and why this is the only kind of "mutation".

E. Why the order in which the development proceeds is essentially the same in all individuals having the same genetic factors.

I will now try to give an explanation of these subjects with the aid of the hypothesis that the genetic factors of development are separately transmittable autokatalytical substances.

A. Why are there two different kinds of factors for the development of an organism, some transmitted through the germ, the others not so transmitted? By some authors this special nature of the genetic factors is ascribed to their vital nature. The chief objection against this view is, as we saw, the inadmissability of explaining the facts of heredity by the action of things which have been invented solely to admit of their being used for an explanation of these facts. This objection can not be made to the proposed hypothesis.

Even admitting the possibility that some external influence could be the cause for the production in an organism of a definite chemical substance, not present before, an even admitting that this substance could reach the germcells, we must see that it would get lost in a succession of generations of cells.

Only if the effect of any influence upon an organism should be such as to produce in that organism a definite autokatalytical compound, could this effect be felt in later generations. And even so, in such a case we should only have the inheritance of this substance, and we have no reason to suppose that in a succeeding generation, the secondary product of e. g. the hypertrophy of an organ by use, could produce an effect in the same direction as the cause for this hypertrophy.

We see therefore, that by the aid of the autokatalysis-hypothesis we can explain the non-inheritance of modifications without recurring to an acceptance of a separation between "germplasm" and "soma", which hypothesis is inferred exclusively from the very facts for the explanation of which it has been invented. The effect of the non-transmitted, the nongenetic factors of development is directly proportionate to the more or less intense action of the influences and their combination.

B. Why are genetic factors inherited independently one from the other? On the autokatalysis-hypothesis this can easily be explained on the assumption that all the different genetic factors of development are simply so many different autokatalytical substances. It does not suffice to assume that for each biotype there is a corresponding autokatalytical substance; in the first place this would be to assume that

there should exist a simply unbelievable large number of these substances, as many as there are different inheritable types of organisms. In the second place, because the unitcharacters of organisms depend, as we have seen, on mutually independently transmitted factors. Each of these factors must therefore be a different compound. In this way we need not assume the existance of so very many different autokatalytical substances, as it are rather the combinations of a relatively small number of genetic factors which give the very many diverse inheritable forms. E. g. we have good reason to believe that the several genetic factors for the production of the coat-colours are absolutely the same in the rabbit, the guinea-pig, the rat and the mouse.

True, even in the range of colour in these diverse groups, there are limitations, due to the fact, that in one form some factor has been lost in several individuals, in other species not, but there must be at least eight or nine factors (for coatcolour alone) which are identical in these animals.

If the parents of a hybrid were different in such a way that n times the one possessed a genetic factor lacking in the other, this hybrid will not produce two different kinds of germcells, but 2^n. The recombination of genetic factors does not take place at the mating of the germcells produced by a hybrid, but at the formation of these germcells. A rabbit, which inherited the genetic factors which are necessary for colour-production, for an interrupted hairgrowth and for long ears, each from only one parent, will distribute each of these things over one half the number of its germcells, so that the result will be, calling the three factors A, B, and C: the production of eight different kinds of gametes, such with A + B + C, with A + B, with A + C, with B + C, with A only, with B only, with C only, and finally such without A, B or C; equal numbers of each of these eight kinds. This is only possible if each factor is capable of independent transmission.

C. An individual which has inherited one genetic factor through only one of its two parents, heterozygote in Mendelian language, usually shows the effect of this factor on its development equally well as one which has inherited this thing from both parents (a homozygote).

In animals notably, one can seldom distinguish a heterozygote from a homozygote (and the few exceptions are of such a nature, as not

to exclude the possibility of a complication through the existence of two factors, which two factors are not yet known separately). This can only mean, that at the moment in development in which the action of the genetic factor is possible, the substance can act as well if the initial amount of it present in the cell is small or large. If the genetic factors for the development are katalyzers for their own formation, this quite covers the facts.

D. Sometimes one of the genetic factors is omitted from a germ-cell produced by an individual which normally furnishes all its gametes with it. We have alredy shown that this kind of spontaneous hereditary variation is the only one which has ever been scientifically demonstrated. On the assumption that the genetic factors for the development are vital particles, it is absolutely impossible to explain how one of them can get lost. On the hypothesis that these factors are independent autokatalytical substances it is very easy to give a plausible explanation.

Any chemical substance can only be produced if materials for its production are at hand. We can very well imagine that by causes outside of the individual some material essential for the formation of some one of these substances can temporarily fail. To give an example: Suppose that oxyde of iron, which has the property of being a ferment for its own formation, be present in an organism. Oxygen is always present in abundance, but we could imagine how, e. g. by an iron-free diet, the quantity of iron present for a continual formation of the oxyde of iron would run short. This must finally result in a distribution of the oxyde of iron present in a given cell over so many cellgenerations, that finally some cells must go without it. If now such cells and their descendants, which would be equally void of the oxyde, would have germcells in their descendance, we would have a spontaneous hereditary variation. Now I do not want to say that oxyde of iron is ever a genetic factor in the development of any organism, but the reasoning must be the same for any other autokatalytical substance.

I must add, that on the assumption of one specific autokatalytic substance for every form of organism, spontaneous hereditary variation would have to be explained by a sudden change from one of these substances into another.

The explanation of the loss of one of the genetic factors from a germcell is thus easily given with the use of the autokatalysis-hypothesis, for the explanation of the acquisition of a genetic factor it would not suffice. But we have seen that we have no reason whatever for the assumption, that spontaneous hereditary variation is ever anything else but the loss of one factor at a time.

Such has been the case in two circumstances of Mutation which it was my good fortune to see in my experiments with mice, under absolute control, one of which instances I published two years ago[1]).

Prof. Baur of Berlin had the kindness to write me that in his experiments with Antirrhinum he had, until now, never witnessed any other kind of mutation but the loss of one single factor at a time. In his cases of mutation, as in mine with mice, every possibility of the production of the new biotype being the result of Mendelian segregation is rigourously excluded.

If I explain the loss of one genetic factor (mutation) by the assumption that something essential for the formation of the autokatalytical substance is temporarily absent in the individual, through circumstances outside of the individual, I must be understood not to say that external influences can have any influence on the production of inheritable differences in the direction in which they act themselves.

E. The order in which the development proceeds, is essentially the same in all individuals having the same genetic factors. For this rule, Haeckel has invented his Biogenetisches Grundgesetz, stating that the ontogenetic development of an organism should be the recapitulation of the phylogenetic development of the form.

The only thing which made it necessary to assume some kind of a mysterious relation between the phylogenetic development of a biotype and the development of its members, was an imperfect insight in the way in which characters of organisms are produced. So long as it was thought or implied, that the development of an organism was a means to produce this organism with all its characters, the analogy

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[1]) Origin of two varieties in Mice by one mutation. University of California Public. Physiology 1908.

could be held. Before a biomechanical view of ontogenesis it will have to give way.

We may not forget that the very facts on which the so-called analogy between phylogeny and ontogeny is based, are valid only in the light of this hypothesis. The touchingly complete series of fossil mammals, which paleontologists want us to recognize as ancestors of the horse is a good example. If somebody had bred these different forms, one from the other, we might speculate upon the causes which made a modern horse's foot show stages of development reminding us of the old Pleiohippus or whatever his name was. But these ancestors have been brought together solely because of the fact that they constitute an unbroken series, and that in the development of the horse some stages remind us of these types.

We have to picture the development of the organism in such a way, that at each stage of development still other factors of development (genetic or nongenetic) can come into play, which until that stage had been forced to remain inactive.

I do not doubt but the hypothesis that the genetic factors for the development of the organism are diverse autokatalytical substances will be a great help in the study of such phenomena as the formation of antitoxins and of functional excitation.

Summary.

1. We can distinguish two kinds of factors for the development of the organisms: genetic factors, transmitted from parent to offspring (Determinationsfaktoren Roux'), and non-genetic factors, the influences of the surroundings in the widest sense (Realisations- and Alterationsfaktoren Roux').
2. Each of the several transmittable genetic factors for the development of an organism is a definite chemical substance which has the property of being a ferment for its own formation (an autokatalyzer).
3. We can distinguish three kinds of variability, which can make children different from their parents:

   A. Modification, the non-inheritable effect of different external postgenetic factors in the development of an individual.

B. Inheritable Variation through Mendelian segregation, caused by a redistribution of genetic factors in the descendants of hybrids between individuals which differ in the possession or non-possession of these factors.

C. Inheritable Variation, caused by the loss of one genetic factor from a gamete, without apparent cause (Mutation).

4. Selection (artificial or natural) can only result in a permanent differentiation the group in which it takes place, when it separates individuals having one or more genetic factors from such as do not have them.

5. Evolution is caused by selection between individuals differing in the innate set of causes for their development, these differences resulting in two ways:

A. By combination of genetic factors in individuals descending from hybrids between different forms, in which they were present.

B. By the loss of a genetic factor from a germcell produced by an individual having it.

Zusammenfassung.

1. Es gibt zwei verschiedene Arten von Faktoren, welche zusammen die Entwicklung der Organismen bestimmen: a) genetische Faktoren, welche von Elter auf Kind übertragen werden (die typischen Determinationsfaktoren Roux'), und b) nichtgenetische Faktoren, welche die Einwirkungen der Umgebung im weitesten Sinne darstellen (Realisationsfaktoren und Alterationsfaktoren Roux').

2. Jeder der vererbten Entwicklungsfaktoren ist ein bestimmter chemischer Stoff, welcher ein Ferment für seine eigene Synthese ist.

3. Es gibt drei Ursachen, welche einen Unterschied zwischen Elter und Kind hervorrufen können:

A. Modifikation. Der nicht erbliche Einfluß verschiedener äußerer Einflüsse, nichtgenetischer Faktoren, auf die Entwicklung.

B. Erbliche Variation, durch Mendelspaltung, verursacht durch die verschiedene Verteilung der genetischen Faktoren auf die

Nachkommen der Hybriden, zwischen Individuen, welche in ihren genetischen Faktoren unterschieden sind.

C. Erbliche Variation durch Verlust eines genetischen Faktors ohne nachweisbare Ursache.

4. Natürliche oder künstliche Zuchtwahl kann nur dann die Form, auf welche sie einwirkt, beständig beeinflussen, wenn durch sie Individuen, welche einen oder mehrere genetische Faktoren haben, von solchen getrennt werden, die sie nicht haben.

5. Evolution wird verursacht durch Zuchtwahl zwischen Individuen, welche in den vererbten Ursachen ihrer Entwicklung verschieden sind. Diese Unterschiede entstehen auf zwei Weisen: durch Mendelspaltung oder durch Verlust eines der genetischen Faktoren.

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